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**3-(Dimethylamino)-5,6,7,8,9,10-hexahydro- 12,13-dimethoxy-4H-spiro[benzo-
1-thia-2,5-diazacyclododecene-4,1'-cyclobutan]-6-one 1,1-Dioxide
Dichloromethane Solvate (1/1) at 173K**

Linden, Anthony ; Mihova, Tonya R ; Heimgartner, Heinz

Abstract: The 12-membered ring in the title compound, C₂₀H₂₉N₃O₅S·CH₂Cl₂, has conformational disorder with the two C atoms adjacent to the fused benzene ring each occupying two sites. The major conformer is present in 74.3(8)% of the molecules. The formal N₂=C bond in the 12-membered ring and the adjacent C-N bond of the dimethylamino substituent have almost identical lengths, indicative of the electron donor character of the dimethylamino group. The amide group has the trans conformation and forms an intramolecular hydrogen bond with one of the sulfonyl O atoms. The solvent molecule forms C-H...O hydrogen bonds with the organic substrate. This novel heterocycle has been formed by a ring enlargement reaction of the corresponding nine-membered 1,2-benzothiazonin-3-one 1,1-dioxide and 2-(dimethylamino)-1-azaspiro[2.3]hex-1-ene.

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3-(Dimethylamino)-5,6,7,8,9,10-hexahydro-12,13-dimethoxy-4*H*-spiro[benzo-1-thia-2,5-diazacyclododecene-4,1'-cyclobutan]-6-one 1,1-Dioxide Dichloromethane Solvate (1/1) at 173 K

ANTHONY LINDEN, TONYA R. MIHOVA AND HEINZ HEIMGARTNER

*Institute of Organic Chemistry, University of Zürich, Winterthurerstrasse 190, CH-8057 Zürich, Switzerland.
E-mail: alinden@oci.unizh.ch*

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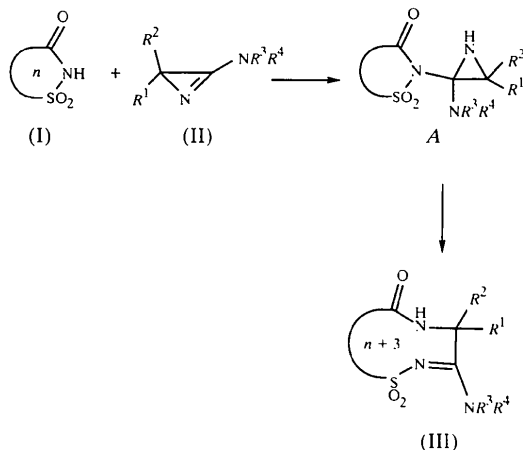
Abstract

The 12-membered ring in the title compound, $C_{20}H_{29}N_3O_5S \cdot CH_2Cl_2$, has conformational disorder with the two C atoms adjacent to the fused benzene ring each occupying two sites. The major conformer is present in 74.3(8)% of the molecules. The formal $N_2=C$ bond in the 12-membered ring and the adjacent C—N bond of the dimethylamino substituent have almost identical lengths, indicative of the electron donor character of the dimethylamino group. The amide group has the *trans* conformation and forms an intramolecular hydrogen bond with one of the sulfonyl O atoms. The solvent molecule forms C—H...O hydrogen bonds with the organic substrate. This novel heterocycle has been formed by a ring enlargement reaction of the corresponding nine-membered 1,2-benzothiazonin-3-one 1,1-dioxide and 2-(dimethylamino)-1-azaspiro[2.3]hex-1-ene.

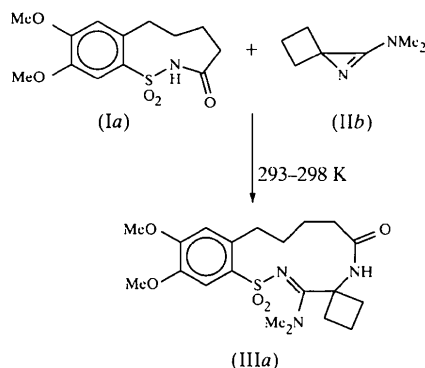
Comment

Cyclic oxosulfonamides of the type (I) and 3-amino-2*H*-azirines, (II), react to give ring-enlarged heterocycles of the type (III) (Heimgartner, 1991; Orahovats *et al.*, 1992, 1996; Villalgordo *et al.*, 1992; Mihova *et al.*, 1996, 1998). This reaction proceeds *via* the formation of an aziridine intermediate, A, and the regioselective nucleophilic attack of the aziridine N atom onto the carbonyl group. This mechanism has been proven in the case of a five-membered starting material, (I), by using ^{15}N -labelled (II) (Ametamey *et al.*, 1988). In some

cases, minor side products were identified, but only one example of a product resulting from the nucleophilic attack of the aziridine N atom of A onto the SO₂ group could be characterized (Rahm *et al.*, 1991).



The speed of the ring enlargement to compound (III) depends strongly on the kind of substituents carried by the azirine, (II), as well as on the ring size of (I). For example, the reaction of 3-(dimethylamino)-2,2-dimethyl-2*H*-azirine ($R^1-R^4 = \text{CH}_3$), (IIa), which is one of the most reactive 3-amino-2*H*-azirines, with four- and five-membered oxosulfonamides, (I), is smooth at room temperature but sluggish with six- to eight-membered homologues of type (I). In the case of the nine-membered starting material, (Ia), only the most reactive aminoazirine, (IIb) [$R^1-R^2 = -(\text{CH}_2)_3-$, $R^3 = R^4 = \text{CH}_3$], led to an addition product, although with a low yield of 8.4% (Mihova *et al.*, 1998). The crystal structure of this novel 12-membered title heterocycle, (IIIa), as its 1:1 solvate with CH₂Cl₂, is now reported



and compared with those of other related cyclic sulfonamidines of type (III). Structures have already been determined for ten compounds with $n = 4-8$, *i.e.* the seven- to eleven-membered heterocycles with various substituents for R^1-R^4 (Rahm *et al.*, 1991; Orahovats *et al.*, 1992, 1996; Villalgordo *et al.*, 1992; Mihova *et al.*, 1996, 1998).

The bond lengths and angles in the title compound have values normally observed in this class of compound. Particularly noteworthy are the lengths of the formal N2=C3 and N3—C3 bonds which are almost identical in (IIIa) and differ by no more than 0.05 Å in the previously reported structures of all other heterocycles of type (III). This delocalization of the formal N2=C3 bond is a result of the electron donor strength of N3. The largest deviations between the lengths of the N2=C3 and N3—C3 bonds are found when a methylphenylamino substituent is present at C3 (Villalgordo *et al.*, 1992; Mihova *et al.*, 1996), because this substituent is a weaker donor than the dimethylamino substituent which is present in all of the other analogues. In (IIIa), the presence of delocalization in this region of the molecule is further supported by the near coplanarity of the atoms on either side of the N2=C3 and N3—C3 bonds, as shown by the respective torsion angles about these bonds (Table 1). A similar coplanarity is found in the related compounds of type (III), where the corresponding torsion angles generally differ from 0 or 180° by less than 20°. Remarkable exceptions to this are found in the structures of four eight-membered analogues (Rahm *et al.*, 1991), where the torsion angles about the formal N2=C3 bond deviate from planar values by between 30 and 42°. This may be the result of conformational constraints which are present exclusively in the eight-membered heterocycles.

The dimethylamino substituent in (IIIa) is tilted slightly towards N2, as shown by the bond angles about C3. This is due to steric interactions between C18 of the dimethylamino substituent and C21 of the cyclobutane ring. The enlarged angle of C3—C4—C21 is also indicative of this interaction. The amide group has the *trans* conformation with the torsion angle C4—N5—C6—C7 = −165.4(3)°. This conformation is found for most of the other ring sizes (Rahm *et al.*, 1991; Orahovats *et al.*, 1992, 1996; Mihova *et al.*, 1998), although the *cis* conformation is found in the seven-membered ring (Mihova *et al.*, 1996) and in one of the eight-membered ring analogues (Villalgordo *et al.*, 1992). The seven-membered ring is clearly too small to allow sufficient puckering for the amide group to attain a *trans* conformation, while for this to occur in the eight-membered ring considerable ring strain is probably necessary because of the constraints introduced by the N2=C3 bond. Those eight-membered analogues that do have the *trans* conformation are the same ones in which there is a considerable out-of-plane twist about the N2=C3 bond, as mentioned above, and have a very puckered-looking ring (Rahm *et al.*, 1991). Indeed, the amide groups in these latter compounds are clearly also under strain as they deviate from a perfect *trans* conformation by between 27 and 38°.

The 12-membered ring in the title compound has conformational disorder involving atoms C9 and C10, resulting in the need to refine two positions for each

of these atoms. One conformation predominates in the crystal with 74.3(8)% of the molecules having this conformation (Fig. 1). The two conformations are essentially related by inverse puckering of the ring between C8 and C11, as shown by the pairs of torsion angles C7—C8—C9/C9a—C10/C10a and C8—C9/C9a—C10/C10a—C11 having similar magnitudes but opposite signs. It was necessary to restrain the lengths of those C—C bonds that involved at least one of the disordered C_i atoms and the largest peaks and holes of residual electron density were also in the vicinity of the disordered atoms. This suggests that this part of the 12-membered ring probably adopts many conformations of similar energy, a phenomenon often observed in large macrocycles. None of the other analogous heterocyclic compounds with different ring sizes exhibits any disorder.

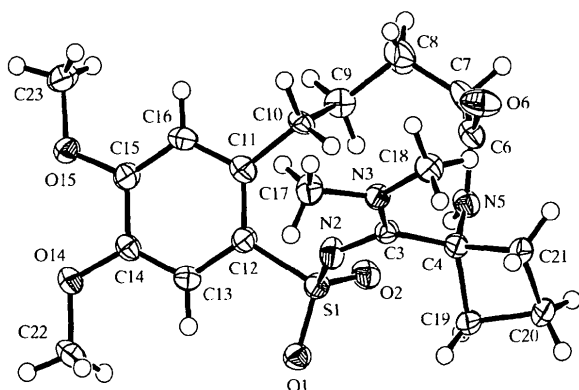


Fig. 1. View of the major conformation of (IIIa) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented by circles of arbitrary size.

The amide group of (IIIa) forms an intramolecular hydrogen bond with one of the sulfonyl O atoms, thereby completing a seven-membered ring. In the analogous compounds with different ring sizes, some structures exhibit similar intramolecular hydrogen bonds, while others display intermolecular interactions which form chains of molecules or dimeric units. There is no correlation between ring size and the hydrogen-bonding motif.

The dichloromethane solvent molecule takes part in C—H...O hydrogen bonds. One of the dichloromethane H atoms forms bifurcated hydrogen bonds with the two methoxy O atoms of (IIIa), while the other H atom interacts with the amide O atom (Table 2). These interactions link pairwise the unique moieties in the structure into infinite one-dimensional chains which run in the [010] direction.

Experimental

The title compound, (IIIa), was obtained in 8.4% yield by stirring a 1:1.5 mixture of 2,3,4,5,6,7-hexahydro-9,10-dimethoxy-1,2-benzothiazonin-3-one 1,1-dioxide, (Ia), and 2-(dimethylamino)-1-azaspiro[2.3]hex-1-ene, (IIb), in acetonitrile at 293–298 K for 65 h (Mihova *et al.*, 1998). Chromatography on silica gel and recrystallization from dichloromethane–ether gave colourless plates (m.p. 517.7–528.1 K).

Crystal data

C₂₀H₂₉N₃O₅S·CH₂Cl₂

M_r = 508.46

Triclinic

*P*1̄

a = 12.112 (2) Å

b = 13.460 (2) Å

c = 7.946 (2) Å

α = 97.72 (2)°

β = 102.21 (2)°

γ = 102.98 (1)°

V = 1211.1 (4) Å³

Z = 2

D_x = 1.394 Mg m^{−3}

D_m not measured

Mo Kα radiation

λ = 0.71069 Å

Cell parameters from 25 reflections

θ = 18.5–20.0°

μ = 0.391 mm^{−1}

T = 173 (1) K

Plate

0.45 × 0.38 × 0.09 mm

Colourless

Data collection

Rigaku AFC-5R diffractometer

ω–2θ scans

Absorption correction:

ψ scan (North *et al.*, 1968)

T_{min} = 0.910, *T_{max}* = 1.000

5827 measured reflections

5565 independent reflections

3797 reflections with

I > 2σ(*I*)

R_{int} = 0.025

θ_{max} = 27.5°

h = 0 → 15

k = −17 → 17

l = −10 → 10

3 standard reflections

every 150 reflections

intensity decay: insignificant

Refinement

Refinement on *F*²

R [*F*² > 2σ(*F*²)] = 0.057

wR (*F*²) = 0.161

S = 1.056

5565 reflections

316 parameters

H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0602P)^2 + 1.4198P]$

where $P = (F_o^2 + 2F_c^2)/3$

(Δ/σ)_{max} = 0.001

Δρ_{max} = 0.76 e Å^{−3}

Δρ_{min} = −0.76 e Å^{−3}

Extinction correction: none

Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. Selected geometric parameters (Å, °)

S1—N2	1.588 (3)	N5—C6	1.356 (4)
S1—C12	1.786 (3)	C3—C4	1.531 (4)
N2—C3	1.326 (4)	C6—C7	1.517 (5)
N3—C3	1.327 (4)	C4—C19	1.565 (4)
N3—C17	1.466 (4)	C4—C21	1.570 (4)
N3—C18	1.465 (3)	C19—C20	1.557 (4)
N5—C4	1.466 (4)	C20—C21	1.544 (4)
O1—S1—O2	114.72 (13)	N5—C4—C3	109.0 (2)
N2—S1—C12	101.10 (14)	C3—C4—C21	123.9 (3)
S1—N2—C3	133.3 (2)	N5—C6—C7	115.5 (3)
C3—N3—C17	118.4 (2)	C6—C7—C8	113.9 (3)

C3—N3—C18	126.6 (2)	C19—C4—C21	86.6 (2)
C6—N5—C4	123.6 (3)	C4—C19—C20	88.4 (2)
N2—C3—N3	114.9 (3)	C19—C20—C21	87.8 (2)
N2—C3—C4	122.5 (2)	C4—C21—C20	88.7 (2)
N3—C3—C4	122.6 (2)		
C12—S1—N2—C3	−135.0 (3)	N3—C3—C4—N5	−107.0 (3)
N2—S1—C12—C11	60.3 (3)	N3—C3—C4—C21	27.8 (4)
S1—N2—C3—N3	168.8 (3)	C4—N5—C6—C7	−165.4 (3)
S1—N2—C3—C4	−11.3 (5)	N5—C6—C7—C8	109.0 (3)
C18—N3—C3—N2	178.3 (3)	C7—C8—C9—C10	96.2 (4)
C17—N3—C3—N2	3.6 (4)	C8—C9—C10—C11	−179.0 (3)
C6—N5—C4—C3	68.1 (3)	C7—C8—C9a—C10a	−87.1 (9)
N2—C3—C4—N5	73.1 (3)	C8—C9a—C10a—C11	175.7 (8)

Table 2. Hydrogen-bonding geometry (Å, °)

D—H...A	D—H	H...A	D...A	D—H...A
N5—H5...O2	0.870 (18)	2.10 (3)	2.773 (3)	133 (3)
C1—H11...O6 ⁱ	0.99	2.23	3.192 (4)	163
C1—H12...O14 ⁱⁱ	0.99	2.33	3.177 (4)	144
C1—H12...O15 ⁱⁱ	0.99	2.42	3.274 (5)	144

Symmetry codes: (i) 1 − x, −y, −z; (ii) 1 − x, 1 − y, −z.

The absorption corrections were based on the ψ scans of three reflections. Two methylene groups, C9 and C10, of the 12-membered ring are disordered. Two positions were defined for each of these atoms and their site occupation factors were refined. The major conformation has an occupancy of 0.743 (8). The conformation of the disordered region was restrained to maintain a reasonable geometry by applying *DFIX* restraints (Sheldrick, 1997) to all C—C bonds involving at least one of the atoms C9 and C10. The largest peaks and holes of residual electron density were 0.87 and 0.38 Å from C11 and C10a, respectively. The amide H atom was placed in the position indicated by a difference electron density map and its positional and isotropic displacement parameters were allowed to refine while the N—H bond length was restrained to 0.90 (2) Å. All of the remaining H atoms were placed in geometrically calculated positions. The methyl H atoms were refined as rigid groups which were allowed to rotate but not to tip, and $U_{\text{iso}}(\text{H})$ was set equal to $1.5U_{\text{eq}}(\text{parent atom})$. All other H atoms were allowed to ride on their parent atoms with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1991). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN PROCESS* (Molecular Structure Corporation, 1989). Program(s) used to solve structure: *SHELXS86* (direct methods) (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL97*. Molecular graphics: *ORTEPII* (Johnson, 1976). Software used to prepare material for publication: *SHELXL97*.

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Highly Rigid Crown Ether Fragments: Phenyl and Cyclohexyl Catechol Ethers

JEFFREY C. BRYAN, JÉRÔME L. LAVIS AND RICHARD A. SACHLEBEN

Chemical and Analytical Sciences Division, Oak Ridge National Laboratory, Oak Ridge, TN 37831-6119, USA.
E-mail: bryanjc@ornl.gov

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Abstract

The structures of 1,2-bis(*o*-nitrophenoxy)benzene [(1), C₁₈H₁₂N₂O₆], 2,2'-*o*-phenylenedioxybis(phenylamine) [(2), C₁₈H₁₆N₂O₂] and *meso*-2,2'-*o*-phenylenedioxybis(cyclohexanol) [(3), C₁₈H₂₆O₄], potential precursors for rigid crown ether molecules, are presented. Each structure displays hydrogen bonding. Compound (1) exhibits weak C—H...O interactions, while (2) and (3) display extensive E—H...E and E—H... π (E = N, O) bonding.

Comment

Much of our recent work with crown ether molecules has focused on the substitution of their relatively flexible ethylene linkages with more rigid groups such as benzo, cyclohexano, or furano (Burns *et al.*, 1996). Making crown ether molecules more rigid will limit their conformational flexibility and can affect their